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Donald E. McClure, Principal Investigator

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Abstract

This report describes the research accomplished under the support of Graduate Research Fellowships at the Center for Intelligent Control Systems, Brown University, during the period July 1989 through June 1991.

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1 Introduction

The fellowship grant DAAL03-89-G-0010 (*Center for Intelligent Control Systems - Brown University Component; Graduate Research Fellowships*) from the U.S. Army Research to Brown University supported the work of two Ph.D. candidates in Applied Mathematics during the period July 1, 1989 through June 30, 1991. Both students were supported for one year each, the final year of their dissertation research. The thesis topics involved research in the broad area of intelligent vision systems supported by ARO contracts to the Center for Intelligent Control Systems (Brown-Harvard-MIT). In both cases, the fellowship support enabled the students to devote their full attention to their research and to produce contributions of the highest quality within the allotted time.

In the two sections that follow, we summarize the accomplishments during the fellowship grant period of Kevin M. Manbeck and Christopher Raphael.

2 Research in Computed Tomography and Ill-Posed Inverse Problems in Image Analysis

Kevin Manbeck received support from this grant during the 1989–90 academic year. His Ph.D. in Applied Mathematics was awarded by Brown University in May 1990. Dr. Manbeck's thesis research was supervised by Professor Stuart Geman.

Previously, members of our research group have pioneered the use of Bayesian statistical methods for emission computed tomography [2], [3]. In the earlier work, however, only limited use was made of data from real clinical emission tomography systems and no experiments were carried out with practical methods for accommodating the affects of photon scattering.

Dr. Manbeck's dissertation [4] emphasizes the use of data from real single-photon-emission-tomography systems and, in his extensions of the Bayesian approach, he develops a semi-empirical approach for compensating for effects of Compton scattering.

An abstract of the thesis follows:

Abstract. *Bayesian Statistical Methods Applied to Emission Tomography with Physical Phantom and Patient Data*, by Kevin Monroe Manbeck, Ph.D., Brown University, May 1990.

In single photon emission computed tomography (SPECT), projection data Y are used to reconstruct an unknown isotope concentration map X . In this

thesis, the physics of SPECT—including photon attenuation, photon scatter, and the Poisson nature of radioactive decay—are modelled in a probabilistic framework, and a physical phantom is used in experiments designed to measure the magnitude of these effects. The experimental results are incorporated into the entries of the discrete attenuated Radon transform \mathcal{A} . The matrix \mathcal{A} specifies the process by which the original image X is transformed into the data Y . The model, studied from a Bayesian perspective, gives rise to a posterior probability distribution $P(X|Y)$. A convenient algorithmic method of using the data Y to estimate X is presented. The algorithm, which iterates conditional expectations (ICE) of the posterior distribution, is implemented in order to reconstruct isotope concentrations. Isotope concentrations are estimated for both patient data and for physical phantom data.

Related Research. Building on the work started in this thesis, S. Geman, K. Manbeck and D.E. McClure have written a Chapter for the forthcoming volume on theory and applications of Markov random fields in image analysis [1].

Dr. Manbeck also participated in research projects concerned with deblurring of Hubble telescope images [5] and with the identification of coronary arteries in digital X-rays of the heart (arteriograms).

The work on recovering images about faint point sources in images affected by aberrations of the Hubble telescope was done in cooperation with scientists at the University of Massachusetts. The inverse problems encountered in deblurring the images are formally similar to the inverse problems

encountered in dealing with Compton scattering in the context of computed tomography.

The work on coronary arteriograms was done in collaboration with Stuart Geman and Dr. Jon Elion, Division of Cardiology, The Miriam Hospital in Providence. That project is continuing and represents a different direction for Manbeck from his thesis. New applications of probabilistically deformable templates are being explored. This particular application, besides being of considerable practical importance in its own right, provides a concrete framework for a variety of object recognition problems in computer vision where essentially one-dimensional structures exhibit considerable variability from instance to instance. The method of dynamic programming is being adapted to effectively find globally optimal solutions of very large scale optimization problems.

An abstract of two lectures presented on this work follows:

Abstract. *The Machine Recognition of Human Coronary Arteries*, by S. Geman, J. Elion and K.M. Manbeck, June 1990.

Arteriography is a medical technique where an x-ray absorbing dye is injected into a patient's arteries. When x-rays are passed through the patient and collected, a medical specialist is able to visually examine the data and diagnose abnormalities such as blocked arteries. Arteriography is often used by cardiologists in order to examine a patient's coronary arteries. Arteriography has proven to be a valuable tool, however, one problem is particularly troublesome. There is a high variability among cardiologists in the interpretation of arteriograms. For this reason, it is desirable to have a consistent,

reliable, machine interpretation of the coronary arteriogram.

There are two sources of variability present in human coronary arteries. The first is the natural variability one would expect between different people, the second comes from the stretching and twisting that occurs as the heart contracts. Even though there is variability, there is also a certain degree of *invariance*. This idea of variability superimposed on an invariant structure brings to mind Grenander's notion of the *deformable template*.

The notion of a deformable template was exploited to design an arteriogram recognition package based on a powerful mathematical model. The modeling process began by specifying several "prototypical" coronary artery structures. The prototype arterial structures, or templates, were studied in a effort to quantify the variability between patients. The prototype images were also used to model the effects of the ribs and lungs which tend to degrade arteriograms.

Once a workable mathematical model of an arteriogram was developed, a recognition algorithm was applied to real patient data. Prototypical templates were deformed into the observed data, and the arteriogram was recognized as that template which most closely matched the data. The process of determining the optimal match was accomplished by a dynamic programming algorithm similar to the ones that have been successfully implemented on the hidden Markov model approach to speech recognition. Based on the optimal template, the arteriogram recognition package segmented and labeled the observed arteriogram into its component parts.

3 Research in Treatment Planning for Radiation Therapy

Christopher Raphael received support from this grant during the 1990–91 academic year. His Ph.D. in Applied Mathematics was awarded by Brown University in May 1991. Dr. Raphael's thesis research was supervised by Professor Donald E. McClure.

Only recently has there been any attempt to carefully model the physical processes in radiation therapy and to use the models for treatment planning. The types of mathematics that arises is a *dual* version of the tomography reconstruction problem. In treatment planning, however, the system of equations that describes a treatment plan may not have a physically realizable solution. Thus one is led to the goal of trying to find a “best” approximate solution among those that are physically realizable.

Dr. Raphael's thesis [7] carefully formulates the treatment planning problem as an optimization problem. The criteria of optimality are considered in terms of their clinical interpretations, as opposed to the mere mathematical convenience.

A summary of his thesis follows:

Summary. *Mathematics in Radiation Therapy Treatment Planning*, by Christopher S. Raphael, Ph.D., Brown University, May 1991.

Ever since Marie Curie's discovery of the value of radium in treating cancer, radiation therapy has been a field of great importance in medicine. In its earlier days, application techniques were crude and the goals of treatment

vague. Since then, CAT scanning procedures have developed which allow the precise differentiation of healthy tissue and tumor. In addition the modern teletherapy machines enable the clinician to deliver clearly delineated and carefully contoured fields of radiation. Now that so much more information and control are available, we feel acutely the need for a mathematical context which supports some notion of optimality in treatment. The main goal of this dissertation is to present this context and examine a wide variety of optimization problems ranging from the mathematically expedient to the most current and biologically motivated.

The basic operator of this thesis, the *dose operator*, describes the relationship between a *treatment plan* and the *dose distribution* it produces. The treatment plan consists of a collection of sources of radiation and an associated collection of intensity profiles—one for each source. A source can be thought of as a point lying somewhere outside the patient while an intensity profile describes the intensities of the various rays which emanate from the source. In practice this profile is controlled by constructing a lead shield of variable thickness. Once the treatment plan has been fixed, various physical phenomena such as attenuation, divergence, and scatter of radiation combine to produce a distribution of dose inside the patient. The dose operator which governs this relationship is linear.

Our first chapter depicts the dose operator in the context of \mathcal{L}^2 . We develop the adjoint operator which is quite similar to the fundamental operator in tomographic medical imaging. The interesting relationship between these two operators leads to some simple yet extremely useful identities which are essential to the later chapters. Also in this chapter we construct our discrete

model which is the framework in which we present our computer experiments. Due to the generality of this chapter, the discrete model is just a special case of the \mathcal{L}^2 theory already treated.

Next we treat the problem of optimization using the ambient \mathcal{L}^2 distance as a measure of optimality. That is, we formulate our notion of an “ideal” dose distribution and try to minimize the \mathcal{L}^2 distance between our potential treatment and this target. The optimization is complicated by the natural positivity constraint on our treatments since it is not possible to deliver a negative quantity of radiation. We look at this optimization first in the case where the sources are *known*. In this case the dose operator is linear and we develop several interesting algorithms which solve the minimization and prove convergence. When the sources are unknown, the dose operator has linear dependence on the intensity profiles but nonlinear dependence on the sources. In this situation we have developed a projection-pursuit-like algorithm for simultaneously choosing the sources and profiles. This algorithm guarantees convergence of the associated dose distributions to the target when we drop the positivity constraint. In the more realistic situation of constrained optimization with *unknown* sources we present a useful and reasonable algorithm but provide no asymptotic results.

Our next effort is to consider optimization of more realistic measures of error than \mathcal{L}^2 distance. We examine two of these. The first formulates the problem as a collection of dose constraints which are not mutually satisfiable. In this setup the object is to satisfy as many constraints as possible (or more accurately a weighted sum over the satisfied constraints). The second formulation attempts to quantify the *probability* of success of a given treatment.

This is computed in terms of the probability of tumor control and the probability of serious complication, both of which we describe in terms of simple and interesting biological models. For both of these measures we combine relaxation techniques with gradient-descent-like algorithms to achieve our optimization. These formulations provide encouraging practical results on the computer by successfully choosing the "correct" treatment philosophy under various assumptions.

This thesis also examines some more theoretical issues pertaining to radiation therapy. In one chapter we consider the consequences of using the familiar Backprojection Operator from medical tomography as a model for the dose operator. This assumption corresponds to disregarding any degradation of the beam as it moves away from its source and assuming that the collection of sources consists of the entire continuum of possibilities. We discuss the inversion theorem of the Radon Transform which gives our ideal dose distribution as a backprojection of a certain treatment. Unfortunately this treatment contains negative values in general. We have examined some possible compromises although the chapter offers more *insight* into the fundamental mathematics of radiation therapy than it offers practical solutions.

A final chapter develops the null spaces of several simple models of the dose operator. In particular we develop the null spaces of the parallel beam model (no divergence), with no attenuation and then with constant attenuation. These null spaces are useful because they allow us to modify a treatment without changing the distribution of dose it produces. This can be used, for instance, to convert a treatment involving negative values into a more positive one, or to distribute dose more evenly over the different sources in a

treatment.

Related Research. Dr. Raphael has started preparation of two manuscripts based on his dissertation [8], [6].

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